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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	

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10/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,435	UMANA ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/14; 7/16/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-286* is/are pending in the application.

4a) Of the above claim(s) *1-29, 35-64, 69-72, 75-81, 96-185, 187, 191-194, 196-205, and 213-286* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-34, 65-68, 73, 74, 82-95, 186, 188-190, 195, and 206-212* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III (claims 30-34, 65-95, 128, 129, 186-212 and 216-227), claims in Group III drawn to β(1,4) N-acetylglucosaminyltransferase III activity (GnT III), the species of mannosidase II as a Golgi localization domain, the species of Fc-mediated cytotoxicity as a species of consequence of expression, and mannosidase II as a species of additional glycosylation enzyme, in the replies filed on 2/14/2007 and 7/16/2007 is acknowledged. The traversal is on the ground(s) that each of the Groups are related, and thus there is no burden to examine all of the claims (i.e. claims 1-286) because of the overlapping subject matter of the Groups. As an example, applicants assert that art relevant on Group III is likely to teach the inventions of Group I and II. This is not found persuasive because whereas the search for each Group may indeed overlap with the search for the other Groups, these searches are not coextensive. Thus, in order to completely search each and every group, as required by the MPEP (see, e.g. §904.03), various and different search strategies for each would have to be devised, performed, and evaluated against the claims in order to ensure the claims are free of the prior art. In applicants example, art teaching, for example, claim 30 (Group III), would likely anticipate claim 1 (Group I), although claim 30 does not necessarily require an isolated nucleic acid sequence, as recited in claim 1. However, this argument presumes art on the methods of claim 30 would be found. If no art on the method claims were found, this does not automatically mean the product claims (e.g. claim 1, and the proteins of Group II) would be free of the art, as it is easy to imagine methods using the products that do not read on claim 30 (e.g. in methods of purifying the fusion proteins, or in studies of protein localization that do not

require the limitations of the method claims, i.e. modification of and/or isolation of a glycosylated protein).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-29, 35-64, 69-72, 75-81, 96-185, 187, 191-194, 196-205, and 213-286 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on 2/14/2007 and 7/16/2007.

Claim Objections

Claims 30-34 are objected to for depending from a non-elected claim (claim 1). The claims all depend from the nucleic acid molecule of claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-32, 34, 65-68, 73, 74, 82-95, 186, 188-190, 195, and 206-212 are rejected under 35 U.S.C. 102(b) as being anticipated by Russell et al (WO 01/29242 A2, 2001) as evidenced by Umana et al (Nat. Biotech., 1999), Shields et al (JBC, 2002), and Lerouge et al (Curr. Pharm. Biotech., 2000).

Russell et al teach modifying the glycosylation of heterologous proteins, such as antibodies, by expression of fusion proteins comprising a post-translational modification enzyme and the "CMS" region of glycosyltransferases or hydrolases located at a desired point in the glycosylation pathway. The CMS region is taught to be the region that determines spatial distribution of a protein in the ER and/or Golgi. See Example 3, beginning on page 69. Russell et al disclose that post-translational modification enzymes include the general use of N-acetylglucosaminyltransferases (page 8, last ¶) and β-1,4 N-acetylglucosaminyltransferase III (GnT-III) specifically (page 52, first ¶). CMS regions to be used are from enzymes that prepare the glycans for subsequent fucosyl and xylosyl addition, such as mannosidase II. See page 69, line 24 to page 70, first full ¶, and Figure 16.

The production of IgG in the system of Russell et al is disclosed on page 3, lines 26-32, as is the use of humanized IgG (e.g. huNR-LU-10, Examples 1 and 3), which was isolated after expression (e.g. page 65, lines 21-24). Russell et al teach that IgG molecules comprise one glycosylated asparagines in the C_H2 domain (page 59), and that plants do not add an α(1,6)-fucose at the proximal GlcNAc, but rather, an α(1,3)-fucose (page 60), Figures 1 and 2). Expression of Gnt-III in the plant cells of Russell et al would inherently lead to an increased proportion of bisected glycans (both hybrid and complex), as this is the function of GnT-III (see Umana et al, in particular page 178, second column), and is not an activity found in plant cells (see Russell et al, in particular Figure 16). Umana et al link the increase in bisected glycans to an increase in ADCC (e.g. Fc-mediated toxicity via Fc-receptor binding, see the abstract, page 176, first column, first full ¶, and Fig. 5). Furthermore, Umana et al teach that the bisection of glycans by GnT-III removes them as substrates for core fucosylation, leading to a higher

proportion of nonfucosylated glycans (page 178, second column). Shields et al teach this lack of fucosylation leads to an increase in FcγRIIIA affinity. Regarding claim 83, the instant specification (¶ [0031] of the published application) teaches FcγRIIIA to be an activating receptor. Regarding claims 92-95, the results of Umana et al indicate that up to 45-50% of the glycans are bisected, non-fucosylated upon expression of GnT-III (¶ linking pages 177-178, and Figures 3 and 4). Thus, the limitations imposed on the protein produced in claims 85-95, for example, are inherent and naturally follow the expression of GnT-III.

Regarding claims 186, 188-190, 195 and 206-211, one interpretation of independent claim 186 encompasses culturing a host cell expressing a GnT-III fusion protein wherein the host cell also expresses endogenous mannosidase II. This is due to the breadth of the claimed subject matter, i.e. there are no limitations as to the source of mannosidase II or host cell, and no definition of "engineered" in the specification. Thus, a reasonably broad interpretation of the claim includes an interpretation wherein the cell has been engineered to express a GnT-III fusion protein and chosen because the cell expresses other enzymes necessary for glycosylation, i.e. mannosidase II. For reason set forth above, the plant cells of Russell et al comprise a fusion protein of GnT-III and the CMS domain of mannosidase II, but plant cells of Russell et al also inherently comprise the mannosidase II enzyme (see passages cited above, and Fig. 1 of Lerouge et al).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made. .

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al (WO 01/29242 A2, 2001) in view of Umana et al (Nat. Biotech., 1999).

The teachings of Russell et al are as set forth above and applied as before. Russell et al do not specifically teach the use of IgG1. Russell et al further teach the advantages of producing antibodies in plants (pages 3-4), such as low cost.

Umana et al teaches the production of IgG1 antibodies, e.g. chCE7, for clinical use in cancer therapy. See the first column, page 176 and the abstract.

The claimed method of modifying the glycosylation profile of an IgG is essentially disclosed by Russell et al with the exception of the IgG1 limitation. The ordinary skilled artisan, seeking a method to produce an IgG1, would have been motivated to use an IgG1 with the IgG production methods of Russell et al because Umana et al teaches IgG1 to be a well known type of IgG, with certain IgG1 antibodies having clinical relevance. It would have been obvious for the skilled artisan to do this because of the known benefit of producing antibodies in plant cells at a low cost, as taught by Russell et al. Given the teachings of the cited references and the level

of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart
Examiner
Art Unit 1633